Non-Technical Abstract

Phase I Trial of Intraperitoneal Administration of an Attenuated Strain (Edmonston Strain) of Measles Virus, Genetically Engineered to Produce CEA, in Patients with Recurrent Ovarian Cancer

Cancer of the ovary is diagnosed in more than 25,400 women in the United States each year and causes the deaths of over 14,500 women annually. Because there is no effective screening method, more than 70% of ovarian cancer cases are diagnosed after the tumor has already spread beyond the ovaries, and in the majority of women the disease will recur despite aggressive initial treatment with surgery and chemotherapy. Once ovarian cancer has recurred, there are no good treatment options. Despite use of salvage chemotherapy, only a minority of women achieve responses and most patients will subsequently progress in a few to several months. There is an urgent need for innovative approaches for the treatment of recurrent ovarian cancer.

Measles virus is an RNA virus. Although the natural, so-called wild type, measles virus can lead to a potentially serious infectious disease, attenuated strains (vaccine strains) of measles virus have an excellent safety record and have resulted in significant decreases in measles incidence and measles mortality world wide. The impetus for examining the antitumor properties of a vaccine strain of measles virus has been published reports in the literature where natural infection with measles virus has been shown to lead in regression of different malignancies. In our laboratories, we have modified the Edmonston vaccine strain of measles virus to express an inert soluble marker peptide (human carcinoembryonic antigen, CEA). The construction of this novel virus variant, which retains its antitumor effect, is vital because it allows us to monitor the activity of the virus by a blood test and, thus, better individualize treatment. Following construction of MV-CEA, we have confirmed that the virus has potent antitumor activity against ovarian cancer, both in laboratory cell lines and animal models. In contrast, it caused minimal damage in normal ovarian surface cells and the normal lining of the abdomen. In this study, we propose to administer escalating doses of the MV-CEA in the abdominal cavity of patients with recurrent ovarian cancer. Ovarian cancer, when it recurs, is confined in the abdomen in more than 85% of patients, thus making this mode of administration an attractive option in this setting. The virus will be administered every four weeks up to six times provided that the patient has had no significant toxicity associated with the prior treatment and the disease has not progressed. The goals of the study are to (a) find the highest safe dose of MV-CEA that can be administered in the abdominal cavity of women with recurrent ovarian cancer, (b) to assess antitumor efficacy in a preliminary fashion, (c) to evaluate the body's immune response against the virus, and (d) to assess the virus's effects in the body using blood, biological fluids, and tissue samples. We plan to escalate the doses of the virus until we determine the maximum safe dose and to include a total of 34 patients.